IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	Jeffrey Lynn Haddox, Roswell Robert Pfister, James Edwin Blalock, and Matteo Villain
Serial No.	:	To be assigned
Filed	:	Herewith
For	:	SYNTHETIC COMPLEMENTARY PEPTIDES AND OPHTHALMOLOGIC USES THEREOF

PRELIMINARY AMENDMENT

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Name: Lisa M. Melanson
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Commissioner for Patents
Washington, D.C. 20231
Att'n: Box Patent Application

Sir:

Please amend the above-identified application as follows:

In the Specification:

Please replace the paragraph at page 1, line 7 with the following:

Cross-reference to Related Application

This patent application is a continuation of co-pending U.S. Application No. 09/521,365, filed March 8, 2000, and entitled "SYNTHETIC COMPLEMENTARY PEPTIDES AND OPHTHALMOLOGIC USES THEREOF", the contents of which are incorporated herein by reference in their entirety, which claims benefit of provisional patent application U.S. Serial number 60/123,409, filed March 9, 1999.

Please replace the paragraph at page 4, line 7 with the following:

The present invention demonstrates an application of the molecular recognition theory, which is the generation of therapeutic agents that may be used to treat disease. Using this approach, a series of complementary peptides for the pro-gly-pro (SEQ ID NO:1) sequence were designed, synthesized, and tested as antagonists of the PMN chemoattractant, N-acetyl-PGP.

Please replace the paragraph at page 9, line 7 with the following:

The neutrophil chemoattractant, –acetyl-PGP, plays a major role in the initiation of polymorphonuclear leukocyte (PMN) invasion into the alkali-injured eye. In the current study, sense-antisense methodology was used to develop complementary peptides as potential inhibitors of N-acetyl-PGP. The polarization assay was used to measure the potential chemotactic response of polymorphonuclear leukocytes to synthetic N-acetyl-PGP, the ultrafiltered tripeptide chemoattractants obtained from alkali-degraded rabbit corneas, or leukotriene B_4. Inhibition was expressed as the peptide concentration required to produce 50% inhibition (ID_{50}) of polarization. Five complementary peptides were tested as potential inhibitors of N-acetyl-PGP: RTR (SEQ ID NO:2), RTRGG (SEQ ID NO:3), RTR dimer, RTR tetramer, and ASA (SEQ ID NO:4) tetramer. In addition, the RTR tetramer and both monomeric peptides (RTR and RTRGG) were tested, separately, for inhibition of the ultrafiltered tripeptide chemoattractants or LTB_4.

In the Claims:

Please cancel Claims 1-9 without prejudice to applicants' right to pursue prosecution of these claims in a later-filed continuation or divisional application.

Please add new Claims 10 and 11 as follows:

10. (new) A pharmaceutical composition for ophthalmologic uses, comprising a complementary peptide having a sequence complementary to proline-glycine-proline (PGP) (SEQ ID NO:1), wherein said complementary peptide is selected from the group consisting of RTR (SEQ ID NO:2), RTRGG (SEQ ID NO:3), RTR dimer, RTR tetramer, RTR octamer, N-acetyl-RTR multimer, short-chain and long-chain fatty acid RTR multimer, RTR multimer using diaminopropionic acid for the core subunit, RTR multimer using diaminobutyric acid for the core subunit, RTR multimer containing a spacer having the formula $NH_2[CH_2]_n$-COOH[n=2[3-aminopropionic acid]....7[8-aminocaprylic acid]], said spacer replacing diglycine spacer, cysteine RTR multimer having a bicyclic structure, and XTR multimer with N-terminal modifications and core subunit modifications, wherein said complementary peptides have dextrorotatory amino acids substituting for the natural levorotatory, and wherein X may be any amino acid.

11. (new) A method of inhibiting polymorphonuclear leukocyte polarization, chemotaxis, and infiltration into tissue activated by a neutrophil chemoattractant in an individual, comprising the step of administering to said individual a pharmaceutical composition for ophthalmologic uses, so as to inhibit polymorphonuclear leukocyte infiltration into tissue, wherein said neutrophil chemoattractant is selected from the group consisting of N-acetyl-PGP, N-acetyl-PGX, N-methyl-PGX, N-methyl-PGP, and small peptide chemoattractants containing proline and glycine, wherein said pharmaceutical composition comprises a complementary peptide having a sequence complementary to proline-glycine-proline (PGP) (SEQ ID NO:1), and wherein X may be any amino acid.